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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,520	03/08/2001	Hideo Iba	423-59	5027

23117 7590 07/28/2005

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EXAMINER	
MCGILLEM, LAURA L	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/800,520	IBA ET AL.	
	Examiner	Art Unit	
	Laura McGillem	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34, 41-46 and 53-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,41-46 and 53-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/8/01* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/214,465.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.0-0

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 4/27/2005, in which several claims were amended (claims 34 and 46) and in which new claims are added (claims 58-69). Claims are 34, 41-46 and 53-69 are now pending.

Receipt is acknowledged of a terminal disclaimer filed 4/27/2005 in response to the obviousness double patenting rejection of claims 34, 41-46 and 53-57.

Priority

It is acknowledged that Applicants have amended the first sentence of the specification to update the status of the parent application to reflect its status as an issued patent. **Applicant has changed the status of the instant application from Divisional to Continuation.**

Claim Objections

Claims 34, 41, 46, 58 and 64 are objected to because of the following informalities: The word destabilizing is misspelled. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46 and 53-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants claim expression vectors comprising a promoter, a recombinase recognition sequence, a selectable drug-resistance gene having an mRNA-destabilizing sequence, a polyA addition signal, a recombinase recognition sequence, a gene encoding a viral structural protein, and a polyA addition signal arranged in this order, which produces a short-lived transcript of the drug-resistance gene and wherein said promoter transcribes the gene encoding a viral structural protein in a prepackaging cell. Applicants claim expression vectors to be expressed in a prepackaging cell comprising a first LTR of a retrovirus genome and a packaging signal, a recombinase recognition sequence, a selectable drug-resistance gene having an mRNA-destabilizing sequence, a polyA addition signal, a recombinase recognition sequence, a foreign gene, and a second LTR of a retrovirus genome, arranged in this order, which produces a short-lived transcript of the drug-resistance gene. The instant expression vectors include the mRNA destabilizing sequence of a c-fos gene and recites embodiments where the drug resistance gene is selected from the group consisting of a neomycin resistance gene, a puromycin resistance gene and a hygromycin resistance gene. Claims are drawn to cells (including prepackaging cells) into which the said expression vectors are transferred and selected with the drug using

the drug resistance gene with an mRNA destabilizing sequence and the gene encoding a viral structural protein (including gag and pol genes) is subsequently expressed.

The rejection of claims 46 and 53-57 is maintained for reasons of record in the previous office action (mailed 11/02/2004) and for reasons outlined below.

Applicants argue that amended claims 34 and 46 include the structural limitations of DNA constructs A and B as described in the specification. Applicants have amended claim 46 to more specifically recite the components of the expression vector. Claim 46 is now directed to an expression vector to be expressed in a prepackaging cell comprising a first LTR of a retrovirus genome and a packaging signal, a recombinase recognition sequence, a selectable drug-resistance gene having an mRNA-destabilizing sequence, a polyA addition signal, a recombinase recognition sequence, a gene encoding a viral structural protein, and a second LTR of a retrovirus genome, arranged in this order, which produces a short-lived transcript of the drug-resistance gene.

Applicant's arguments filed 4/27/2005 have been fully considered but they are not persuasive. In order to overcome the rejection under 35 U.S.C. 112, first paragraph, claim 46 was amended to further limit the components of the expression vector to comprise a first LTR of a retrovirus genome and a packaging signal, a recombinase recognition sequence, a selectable drug-resistance gene having an mRNA-destabilizing sequence, a polyA addition signal, a recombinase recognition sequence, a gene encoding a viral structural protein, and a second LTR of a retrovirus genome. However, an expression vector comprised of a first and second LTR sequence in combination with

a viral structural gene is also not included as one of the embodiments disclosed in the specification. The instant specification discloses only LTR sequences in combination with foreign genes in DNA construction B for regulating the expression of a foreign gene (see specification page 8-11, in particular) and not LTR sequences with a viral structural gene. The limitations imposed by the amendment of claim 46 are impermissible NEW MATTER.

It is noted that claims 34 and 46 have been amended to remove the preamble phrase "expression vector for a gene encoding a viral structural gene", which read on an expression vector which did not actually recite that the gene encoding the viral structural gene was present in the vector.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 58-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 58-69 are vague and indefinite in that the metes and bounds of the terms "foreign gene" are unclear. The terms are not clearly described in the specification and it is unclear with regard to what the gene or gene product is supposed to be foreign. It would be remedial to amend the claim language to clearly indicate what is intended by the cited terms. **These are new rejections that are**

necessitated by the applicants' amendment of the claims in the response filed 4/27/2005.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 34, 41-45 and 64-69 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2, 6-7, 13, 16, 20 and 22-23 of U.S. Patent No. 6,743,620. Although the conflicting claims are not identical, they are not patentably distinct from each other because as stated in the Office action mailed 11/02/2004, the nature of the invention has changed to such a degree that the claimed invention can no longer be grouped as part of the invention elected by original presentation (i.e. Group II, original claims 8-9, see page 4 of applicants' preliminary amendment filed 3/8/2001). The originally elected invention was directed to a short-lived transcript drug resistance gene characterized by having a base sequence of a short-lived neomycin resistance gene, puromycin resistance gene or

hygromycin resistance gene. The most recent amendments to the claims (filed 4/27/2005) further limit the pending claims to read on expression vectors used to generate prepackaging cells for eukaryotic viral vectors and, as such, are grouped along with the invention prosecuted in the parent application, U.S. Application Serial No. 09/214,465 (now U.S. Patent No. 6,743,620). For this reason, it is now proper to analyze the pending claims with regard to Obviousness-type Double Patenting over the issued claims of the parent application. **These are new rejections necessitated by amendment filed 04/27/2005.**

Claims 34 and 41-45 of the instant application are directed to an expression vector comprising a promoter, a recombinase recognition sequence, a selectable drug-resistance gene having an mRNA-destabilizing sequence, a polyA addition signal, a recombinase recognition sequence, a gene encoding a viral structural protein, and a polyA addition signal arranged in this order, which produces a short-lived transcript of the drug-resistance gene and wherein said promoter transcribes the gene encoding a viral structural protein in a prepackaging cell. Claims 64-69 of the instant application are directed to expression vectors to be expressed in a prepackaging cell comprising a first LTR of a retrovirus genome and a packaging signal, a recombinase recognition sequence, a selectable drug-resistance gene having an mRNA-destabilizing sequence, a polyA addition signal, a recombinase recognition sequence, a foreign gene, and a second LTR of a retrovirus genome, arranged in this order, which produces a short-lived transcript of the drug-resistance gene. The instant expression vectors include the mRNA destabilizing sequence of a c-fos gene and recites embodiments where the drug

resistance gene is selected from the group consisting of a neomycin resistance gene, a puromycin resistance gene and a hygromycin resistance gene. Claims are drawn to cells (including prepackaging cells) into which the said expression vectors are transferred and selected with the drug using the drug resistance gene with an mRNA destabilizing sequence and the gene encoding a viral structural protein (including gag and pol genes) is subsequently expressed.

Claims 1, 6-7,13, 16, 20 and 22-23 of the '620 patent are directed to a DNA construct for regulating expression of a sequence encoding a viral structural protein that is cytotoxic, comprising a promoter, a recombinase recognition sequence, a drug resistance gene, a polyA addition signal, a recombinase recognition sequence, the viral structural protein gene and a polyA addition signal, arranged in this order and operatively linked such that recombination between the recombinase recognition sequences results in the expression of the viral structural protein gene. The drug resistance gene can encode a short-lived transcript that results in neomycin drug resistance, puromycin drug resistance or hygromycin drug resistance (e.g. claims 6-7).

Claims 2, 6-7,16, 20, and 22-23 of the '620 patent are directed to a DNA construct for regulating expression of a sequence encoding a foreign gene which encodes a cytotoxic protein, comprising a first LTR of a retrovirus genome and a packaging signal, a recombinase recognition sequence, the foreign gene which encodes the cytotoxic protein, and a second LTR of a retrovirus genome, arranged in this order, which are operatively linked such that recombination between the

recombination recognition sequences results in the expression of the foreign gene which encoded the cytotoxic protein being regulated by the first LTR.

The DNA construct of claims 1, 6-7, 16, 20, 22 and 23 reads on the expression vector of instant claims 34, and 41-45 which regulates the expression of the viral structural protein by producing a short lived transcript of the drug resistance gene upstream from the gene encoding a viral structural protein. The expression vector of instant claim 34 and 41-45 comprises the recombinase recognition sequences recited in claim 1 of Patent '620 therefore, it would be obvious that recombination between the recombinase recognition sequences of the expression vector of instant claim 34 would result in expression of viral structural protein gene.

This DNA construct of claims 2, 6-7, 16, 20, 21 and 23 reads on the expression vector of instant claims 64-69 which regulates the expression of a foreign gene by producing a short lived transcript of the drug resistance gene upstream from the gene encoding a foreign gene. The expression vector of instant claims 64-69 comprises the recombinase recognition sequences recited in claim 2 of Patent '620 therefore, it would be obvious that recombination between the recombinase recognition sequences of the expression vector of instant claims 64-69 would result in expression of foreign gene.

A prepackaging cell for producing a retrovirus gag/pol gene can be produced by inserting the DNA construct of claims 1 and 6-7 in Patent '620 into prepackaging cells expressing retroviral gag/pol and used to produce retroviral particles comprising the viral structural gene product. In this process, a retrovirus is produced which express viral structural protein genes. The process for producing the prepackaging cell and the

retrovirus comprising viral structural proteins reads on the process for producing cells and for expressing a gene recited in instant claims 43-46 in which expression vectors of claims 34, 41-42 are transferred into cells, selected for drug resistance (prepackaging) and then the viral structural gene is produced in the prepackaging cells.

A prepackaging cell for producing a foreign gene can be produced by inserting the DNA construct of claim 2 and 6-7 in Patent '620 into prepackaging cells expressing retroviral gag/pol and used to produce retroviral particles comprising the foreign gene product. In this process, a retrovirus is produced which expresses foreign gene. The process for producing the prepackaging cell and the retrovirus comprising foreign gene reads on the process for producing cells and for expressing a gene recited in instant claims 68-69 in which expression vectors of claims 64-66 are transferred into cells, selected for drug resistance (prepackaging) and then the foreign gene is produced in the prepackaging cells.

Conclusion

All rejections not mentioned in this Office Action are withdrawn. No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Laura McGillem
7/22/2005

DAVID GUZO
PRIMARY EXAMINER